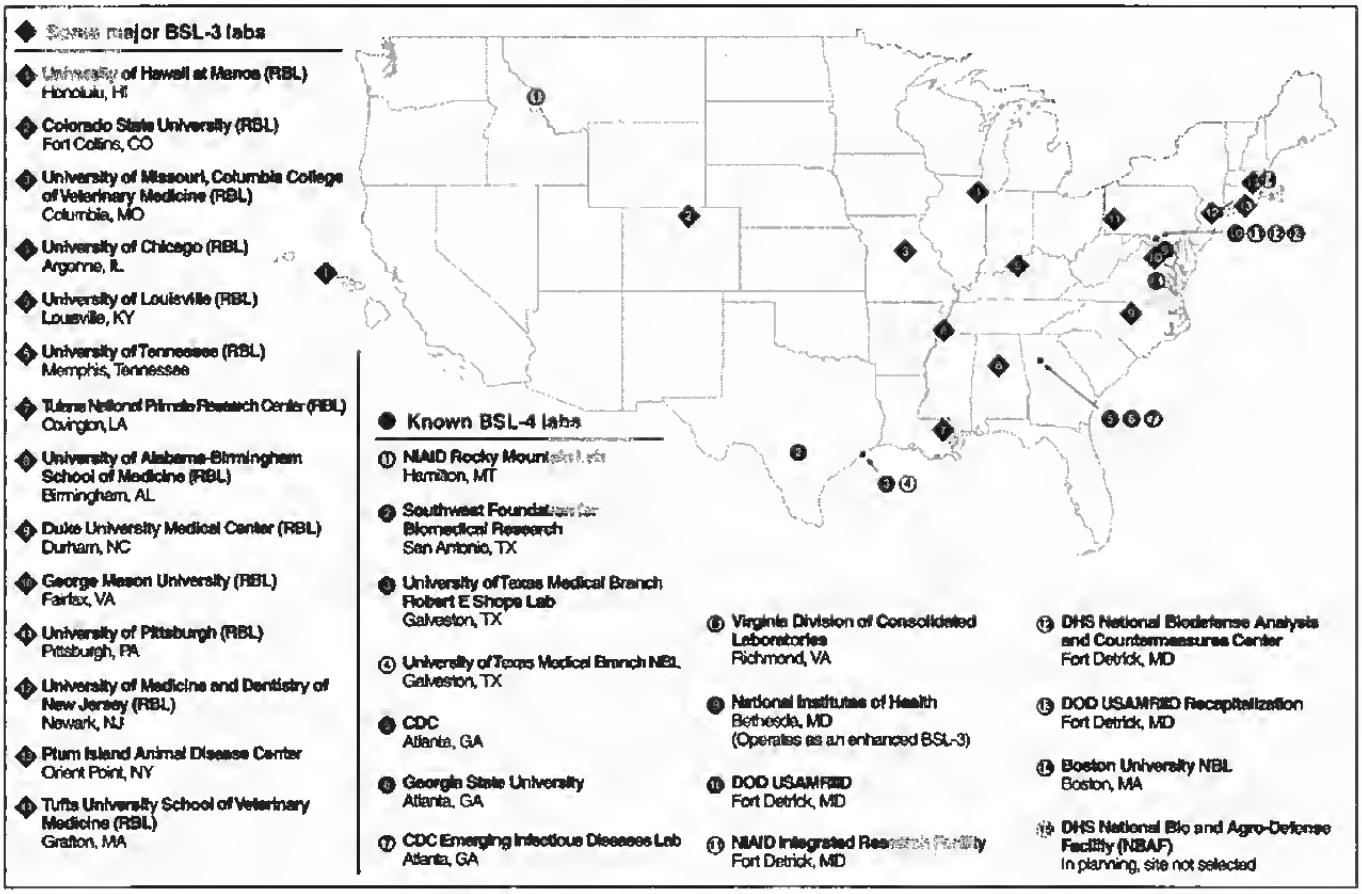
Figure 1: Known BSL-4 Labs and Some of the Major BSL-3 Labs in the United States



◆ Major BSL-3 lab
① Known BSL-4 lab is under construction
② Known BSL-4 lab has been built but is not yet operational
● Known BSL-4 lab is operational
③ Known BSL-4 lab is in planning, site not selected

Source: NIAID and open source.

No Federal Agency Has the Mission to Track High-Containment Labs in the United States

No single federal agency has the mission to track and determine the risk associated with the expansion of BSL-3 and BSL-4 labs in the United States, and no single federal agency knows how many such labs there are in the United States. Consequently, no one is responsible for determining the aggregate risks associated with the expansion of these high-containment labs.

None of the federal agencies that responded to our survey indicated that they have the mission to track and know the number of BSL-3 and BSL-4 labs within the United States (see table 4).

Table 4: Federal Agencies' Mission to Track and Know the Number of All BSL-3 and BSL-4 Labs within the United States

Agency	Mission to track	Know the number
Department of Commerce	No	No
Department of Defense	No	No
Department of Energy	No	No
Department of Health and Human Services	No	No
Department of Homeland Security	No	No
Department of Interior	No	No
Department of Justice	No	No
Department of Labor	No	No
Department of State	No	No
Department of Veterans Affairs	No	No
Environmental Protection Agency	No	No
U.S. Department of Agriculture	No	No

Source: GAO Survey of Federal Agencies Involved with BSL-3 and BSL-4 Labs, 2007.

Some federal agencies do have a narrow mission to track a subset of BSL-3 and BSL-4 labs, and they do know the number of those labs. For example, the CDC and USDA together know the number of high-containment labs working with select agents because, by federal regulation, such labs are required to register with them. But these regulations only require that the entities registering with the Select Agent Program do a risk assessment of their individual labs. No agency, therefore, has the mission to determine the aggregate risks associated with the expansion of high-containment labs that work with select agents. According to the federal agency officials, the oversight of these labs is fragmented and relies on self-policing.

While the number and location of all BSL-3 and BSL-4 labs is not known, several federal agencies indicated that they have a need to know this information in support of their agency missions. Some intelligence agencies, for example, indicated that they need to know a subset of the number and location of high-containment labs within the United States because these labs represent a capability that can be misused by terrorists or people with malicious intent.[7] Without knowledge of the number and location of the BSL-3 and BSL-4 labs, some agencies' work is made more difficult. For example, the FBI has a need to know the number and location of BSL-3 and BSL-4 labs for forensic purposes. Without this information, the FBI's work is made more difficult.

According to the experts, there is a baseline risk associated with any high-containment. With expansion, the aggregate risks will increase. However, the associated safety and security risks will be greater for new labs with less experience. In addition, high-containment labs have health risks for individual lab workers as well as the surrounding community. According to a CDC official, the risks due to accidental exposure or release can never be completely eliminated, and even labs within sophisticated biological research programs—including those most extensively regulated—have had and will continue to have safety failures. In addition, while some of the most dangerous agents are regulated under the CDC-USDA's Select Agent Program, many high-containment labs work with agents not covered under this program. Labs outside the Select Agent Program also pose risks, given that many unregulated agents can cause severe illness or even death (see appendix IV for a list of some agents, but not select agents, recommended to be worked on in high-containment labs). These labs also have associated risks because of their potential as targets for terrorism or theft from either external or internal sources. Even labs outside the Select Agent Program can pose security risks in that such labs represent a capability that can be paired with the necessary agents to become a threat. While the United States has regulations governing select agents, many nations do not have any regulations governing the transfer or possession of dangerous biological agents.

[7]Some intelligence agencies have a mission to track and a need to know the number of all BSL-3 and BSL-4 labs or equivalent abroad. However, they do not know the total number of those labs.

Lessons Learned from Three Recent Incidents Highlight the Risks Inherent in the Expansion of High-Containment Labs

We identified six lessons from three recent incidents: failure to report to CDC exposures to select agents, in 2006, by TAMU (see appendix V); power outage at CDC's new BSL-4 lab, in 2007; and the release of foot-and-mouth disease virus, in 2007, at Pirbright, the U.K. These lessons highlight the importance of (1) identifying and overcoming barriers to reporting in order to enhance biosafety through shared learning from mistakes and to assure the public that accidents are examined and contained; (2) training lab staff in general biosafety as well as in specific agents being used in the labs to ensure maximum protection; (3) developing mechanisms for informing medical providers about all the agents that lab staff work with to ensure quick diagnosis and effective treatment; (4) addressing confusion over the definition of exposure to aid in the consistency of reporting; (5) ensuring that BSL-4 labs' safety and security measures are commensurate with the level of risk these labs present; and (6) maintenance of high-containment labs to ensure integrity of physical infrastructure over time.

Identifying and Overcoming Barriers to Reporting

While the Select Agent Program and the rDNA Guidelines have reporting requirements, institutions sometimes fail to report incidents. According to CDC, there were three specific types of incidents that TAMU officials failed to report to CDC: (1) multiple incidents of exposure, including illness; (2) specific types of experiments being conducted by researchers; and (3) missing vials and animals.

In addition, in November 2006, during our first visit to TAMU—a meeting in which all key officials who knew about these incidents were present—we asked if there had been any incident in which a lab worker was exposed to a select agent. TAMU officials did not disclose any of these incidents. Moreover, in August 2007, during our second visit, the biosafety officer said that he had conducted an investigation of the incident, in which the lab worker was exposed to *Brucella*, and wrote a report. However, the report that was provided to us was dated June 17, 2006, but discussed other incidents that had occurred in 2007, a discrepancy that TAMU failed to explain to us.[8]

[8]The biosafety officer at TAMU told us the following: He had no training in biosafety but was an industrial hygienist by education and experience. He was asked to take on the additional duty of biosafety officer when the previous biosafety officer retired. He was also designated as an alternate responsible officer (RO) but did not know what duties he had to perform as an alternate RO.

According to the literature and discussion with federal officials and experts, accidents in labs are expected, mostly as a result of human error due to carelessness, inadequate training, or poor judgment. In the case of theft, loss, occupational exposure, or release of the select agent, the lab must immediately report certain information to CDC or USDA. However, there is a paucity of information on barriers to reporting by institutions. It has been suggested that there is a disincentive to report acquired infections and other mishaps at research institutions because of (1) negative publicity for the institution or (2) the scrutiny from a granting agency, which might result in the suspension of research or an adverse effect on future funding.[9] Further, it is generally believed that when a worker acquires an infection in the lab, it is almost always his or her fault, and neither the worker nor the lab is interested in negative publicity.

In order to enhance reporting, barriers need to be identified and targeted strategies need to be applied to remove those barriers. It is also important that these incidents be analyzed so (1) biosafety can be enhanced through shared learning from mistakes and (2) the public may be reassured that accidents are thoroughly examined and contained. One possible mechanism for analysis, discussed in the literature, is the reporting system used for aviation incidents, administered by the National Transportation Safety Board and the Federal Aviation Administration.[10] When mistakes are made, they are analyzed and learned from without being attributed to any one individual. Experts have agreed that some form of personal anonymity would encourage reporting.

Training Lab Staff in General Biosafety, as well as in Specific Agents Being Used in the Labs

Training is a key requisite for safe and secure work with dangerous agents. Moreover, it is important that this training is specific to the agent to be worked with and activities to be performed.

The lab worker at TAMU who was exposed was not authorized to work with *Brucella* but was, we were told, being escorted in the lab only to help

[9]High-Containment Biodefense Research Laboratories, Meeting Report and Center Recommendations, *Biosecurity and Bioterrorism*, vol. 5, 1 (New Rochelle, N.Y.: March 2007).

[10]Department of Transportation, Federal Aviation Administration, *FAA Procedures for Handling National Transportation Safety Board Recommendations* (Washington, D.C.: Federal Aviation Administration, March 22, 1995). Also see Federal Aviation Administration, *Accident and Incident Data* (Washington, D.C.: Federal Aviation Administration, Sept. 29, 2006).

out with the operating of the aerosolization chamber.[11] According to the select agent regulations, all staff are required to be trained in the specifics of any agent before they work with it. However, the worker did not receive training in the specifics of *Brucella*, including its characteristics, safe handling procedures, and potential health effects. While the worker was experienced in general BSL-3 procedures, her normal work regimen involved working with *Mycobacterium tuberculosis*, and her supervisor surmised that the differential potential for infection from *Brucella* was partially to blame for the exposure.[12]

In particular, the exposed lab worker was highly experienced in handling *M. tuberculosis*, an infectious agent. A lab director of a BSL-2 lab for the last 5 years, she had a PhD in medical sciences and was, by many accounts, highly competent and reliable. She had applied the procedures governing safe work with *M. tuberculosis* to the *Brucella* experiment. However, her experience with *M. tuberculosis* might have provided a false sense of security.

Had training been given in *Brucella*, the worker might have been more aware when cleaning the aerosol chamber. Typical routes of infection differ between *M. tuberculosis* and *Brucella* and normal procedures, including gowning and respiratory equipment, vary between the two agents. For example, the lab worker wore protective glasses, but they were not tight fitting. This was adequate when working with *M. tuberculosis*, but not with *Brucella*. The investigation concluded that the agent entered the lab worker through the eyes.

According to one expert who has managed high-containment labs, there are risks working alternately in BSL-2 and BSL-3 labs, with their different levels of procedures and practices. The fear is that lab workers may develop a routine with BSL-2 procedures that might be difficult to consciously break when working with the more dangerous agents and activities requiring BSL-3 containment.

[11]According to the CDC, regardless of escort, since the lab worker was not authorized to work with *Brucella*, having the lab worker help out with the aerosolization chamber during the *Brucella* experiments constituted unauthorized access to a select agent and violated the regulations.

[12]Although a person typically has to breathe in *M. tuberculosis* bacteria to get an infection, *Brucella* can enter the system through mucous membranes such as those in the eyes. During the experiment, the lab worker who got exposed had been wearing a respirator that filtered the air she breathed as is recommended for work with *M. tuberculosis*.

Developing Mechanisms for Informing Medical Providers about All the Agents that Lab Staff Work with

Severe consequences for the worker can result from delays in (1) recognizing when an exposure has occurred or (2) medical providers' accurately diagnosing any resulting infection. Further, if the worker acquires a disease that is easily spread through contact, there can also be severe consequences for the surrounding community.

In the *Brucella* incident at TAMU, at the time of the exposure on February 9, 2006, the lab worker did not know she was infected nor did anyone else in the lab. In fact, the CDC conducted a routine inspection of TAMU on February 22, 2006—13 days after the exposure—but had no way of knowing that it had happened. According to the exposed worker, it was more than 6 weeks after the exposure that she first fell ill. Then, the first consultation with her physician indicated that she had the flu; it was only after the symptoms persisted that a consultation with an infectious disease specialist confirmed that her blood contained an unknown microorganism. It was at this point that she recalled her work with *Brucella* weeks earlier. Confirmation of infection with brucellosis was made on April 16, 2006, by the Texas State Public Health Lab—62 days after the exposure. During much of this time, the worker had resumed her normal activities, interacting with many people.

In fact, the exposed lab worker had become seriously ill and the delay in recognizing her infection as brucellosis aggravated her condition. Such misdiagnosis is not uncommon with infectious diseases, as the initial symptoms often appear flu-like and brucellosis is not generally endemic in the population. If the worker had not recalled the experiment with *Brucella* and alerted her physician to this fact, according to the CDC, she might have developed an even more severe infection, possibly affecting her central nervous system or the lining of her heart.

In this incident, it was also fortunate that the disease was such that transmission beyond the initial exposed individual was difficult and that there were no risk of spread to the surrounding community. While brucellosis is not easily transferred between humans, many agents cause diseases that are easily transferred from human to human through coughing or fluid transfer, including some agents that are not select agents, such as SARS and tuberculosis.

According to BMBL, the causative incident for most laboratory-acquired infections is often unknown. It can only be concluded that an exposure took place after a worker reports illness—with symptoms suggestive of a disease caused by the relevant agent—some time later. Since clinical symptoms can take weeks to become apparent, during which time an

infected person may be contagious, it is important that exposure be identified as soon as possible and proper diagnosis and prompt medical treatment provided.

Addressing Confusion over the Definition of Exposure

In addition to the incident of exposure to *Brucella*, the CDC noted several incidents of potential exposure to *Coxiella burnetii* that TAMU had failed to report. While the *Brucella* exposure eventually became apparent because of clinical symptoms in the lab worker, the *C. burnetii* incidents illustrate situations where the determination of exposure can be more problematic. In attempting to address the failure to report, questions were raised about what constitutes sufficient evidence of an exposure that the entity must report to the CDC.

One indication of exposure that can be used for *C. burnetii* and other agents is to periodically measure the titer levels—antibody levels—within the blood serum of lab workers working with those agents. If a person has a raised level over his or her baseline level, then a conclusion can be drawn that the person has been exposed to the agent. However, there are issues with using titer levels as an indication of exposure. For example, determining when the exposure took place is not straightforward.

TAMU has a program of monitoring blood serum for workers with *C. burnetii*—a select agent and the causative agent for Q fever in humans. While humans are very susceptible to Q fever, only about one-half of all people infected with *C. burnetii* show signs of clinical illness. During the CDC's February 22, 2007, inspection, triggered by the uncovering of the *Brucella* incident, it came across clinical records that showed that several lab workers were found to have elevated titers for *C. burnetii*. But no reports had been sent to the CDC. The CDC noted this issue and, on April 24, 2007, TAMU submitted the required Form 3 to report the possible exposure.

However, as a result of subsequent discussion with the individuals who had the elevated titers, TAMU officials began to have doubts about whether or not the elevated titers resulted from exposures that had occurred at TAMU. In one case, TAMU said, one of the infected lab workers had only recently been hired by TAMU but had worked in a clinical lab in China, where *C. burnetii* was known to have been present. In another, the worker claimed to have been exposed many years earlier and had always registered high, although the actual levels varied. CDC officials disagree with this interpretation and believe the high titers resulted from exposures at TAMU.

TAMU initially responded to the uncovering of the elevated titer incidents by reporting, to the CDC, any subsequent elevated titer level uncovered in any of their lab workers. But TAMU is now unsure how to proceed. It has notified the CDC that, in its opinion, an exposure suggested by an elevated titer should be defined to have occurred only after clinical symptoms appear in the individual. TAMU has, therefore, ceased reporting incidents of merely elevated titers. In the absence of clarity over the definition of exposure, TAMU officials have chosen to define it as they see fit.

When we asked the CDC about the confusion over the definition of an exposure, officials agreed that terms need to be clearly defined and are drafting new guidance. CDC officials noted, however, that it is unwise to wait until clinical symptoms appear before determining that an exposure has taken place, as this could potentially endanger a worker's life and, potentially, in the case of a communicable disease, others.

Experts have told us that correctly interpreting the meaning of elevated titers—whose characteristics can vary by agent, host, and testing lab—is challenging since many serological testing methods have not been validated. Gaps in the scientific understanding of infectious diseases—such as the meaning of elevated titers—may become more problematic as the expansion of labs continues. The development of scientifically sound and standardized methods of identifying exposure is critical, so that individual lab owners are not left to determine for themselves what is and what is not reportable.

Ensuring that BSL-4 Labs' Safety and Security Measures Are Commensurate with the Level of Risk These Labs Present

An hour-long power outage, in June 2007, at the CDC's newest BSL-4 facility raised questions about safety and security, as well as the backup power system design. The incident showed that, even in the hands of experienced owners and operators, safety and security of high-containment labs can still be compromised. The incident also raises concerns about the security of other similar labs being built around the nation.

On June 8, 2007, the CDC campus in Atlanta experienced lightning strikes in and around its new BSL-4 facility, and both primary and backup power to that facility failed. The facility was left with only battery power—a condition that provides limited power for functions such as elevators and emergency lighting to aid in evacuation. Among other things, the outage shut down the negative air pressure system, one of the important components in place to keep dangerous agents from escaping the containment areas. In looking into the power outage, the CDC determined

that, some time earlier, a critical grounding cable buried in the ground outside the building had been cut by construction workers digging at an adjacent site. The cutting of the grounding cable, which had gone unnoticed by CDC facility managers, compromised the electrical system of the facility that housed the BSL-4 lab.[13]

According to CDC officials, the new BSL-4 facility is still in preparation to become fully operational and no live agents were inside the facility at the time of the power outage. However, given that the cable was cut, it is apparent that the construction was not supervised to ensure the integrity of necessary safeguards that had been put in place.

Further, according to CDC officials, it was not standard procedure to monitor the integrity of the electrical grounding of the new BSL-4 facility. However, CDC has now instituted annual testing of the electrical grounding system.

Because of the power outage incident, questions about the design of the backup power system for the new facility resurfaced. When the CDC designed the backup power system for the new BSL-4 facility, it used backup generators at a central utility plant which serve other facilities, as well as functions such as chillers, on campus besides the new BSL-4 facility. According to internal documents provided to us, during design phase for the facility, some CDC engineers had questioned the remotely placed, integrated design rather than a simpler design using local backup generators near the facility. These engineers warned that the backup power system would not adequately protect the BSL-4 facility from failing in certain scenarios, including an outage due to a lightning strike.

According to CDC facility officials, the full backup power capabilities for the new BSL-4 facility are not in place yet, but are awaiting completion of other construction projects on campus. Once these projects are completed, these officials said, the new BSL-4 facility will have multiple levels of backup power, including the ability to get power from a second central utility plant on campus, if needed. But some CDC engineers that we talked to questioned the degree of complexity in the design. They are worried that an overly integrated backup might be more susceptible to failure. As a result of this power outage incident, CDC officials said, the

[13]A subsequent third-party investigation determined that the grounding of another building housing CDC's older BSL-4 labs was also compromised in a similar fashion.

CDC is doing a reliability assessment for the entire campus power system, which will include the backup power design for the new BSL-4 facility.

Some experts have suggested that BSL-4 labs be similar in design to a nuclear power plant, with a redundant backup-to-backup power system, along with adequate oversight. Like such plants, BSL-4 labs are considered targets for terrorists and people with malicious intent. Release of an agent from any of these labs could have devastating consequences. Therefore, appropriate design of labs and adequate oversight of any nearby activities—such as adjacent construction with its potential to compromise buried utilities—are essential.

Maintenance of High-Containment Labs

High-containment labs are highly sophisticated facilities, which require specialized expertise to design, construct, operate, and maintain. Because these facilities are intended to contain dangerous microorganisms, usually in liquid or aerosol form, even minor structural defects—such as cracks in the wall, leaky pipes, or improper sealing around doors—could have severe consequences. Supporting infrastructure, such as drainage and waste treatment systems, must also be secure.

In August 2007, contamination of foot-and-mouth disease was discovered at several local farms near Pirbright in the U.K., the site of several high-containment labs that work with live foot-and-mouth disease virus. Foot-and-mouth disease is one of the most highly infectious livestock diseases and can have devastating economic consequences. For example, a 2001 epidemic in the U.K. cost taxpayers over £3 billion, including some £1.4 billion paid in compensation for culled animals.[11] Therefore, the U.K. government officials worked quickly to contain and investigate this recent incident.

The investigation of the physical infrastructure at the Pirbright site found evidence of long-term damage and leakage of the drainage system servicing the site, including cracked and leaky pipes, displaced joints, debris buildup, and tree root ingress. While the definitive cause of the release has not been determined, it is suspected that contaminated waste water from Pirbright's labs leaked into the surrounding soil from the deteriorated drainage pipes and that live virus was then carried offsite by vehicles splashed with contaminated mud.

[11]Department for Environment, Food, and Rural Affairs, *Foot and Mouth Disease: Applying the Lessons* (London, U.K.: National Audit Office, Feb. 2, 2005).

The cracked and leaky pipes found at Pirbright are indicative of poor maintenance practice at the site. The investigation found that (1) monitoring and testing for the preventative maintenance of pipework for the drainage system was not a regular practice on site and (2) the investigation found that a contributing factor might have been a difference of opinion over responsibilities for maintenance of a key pipe within the drainage system.

High-containment labs are expensive to build and expensive to maintain. Adequate funding for each stage needs to be addressed. Typically, in large-scale construction projects, funding for initial construction comes from one source. But funding for ongoing operations and maintenance comes from somewhere else. For example, in the NIAID's recent funding of the 13 BSL-3 labs as RBLs and 2 BSL-4 labs as National Biocontainment Labs (NBL), the NIAID contributed to the initial costs for planning, design, construction, and commissioning. But the NIAID did not provide funding to support the operation of these facilities. In this case, the universities themselves are responsible for funding any maintenance costs after initial construction.

The Pirbright incident shows that beyond initial design and construction, ongoing maintenance plays a critical role in ensuring that high-containment labs operate safely and securely over time. Because even the smallest of defects can affect safety, ensuring the continuing structural integrity of high-containment labs is an essential recurring activity.

Concluding Observations

The expansion of BSL-3 and BSL-4 labs taking place in the United States is proceeding in a decentralized fashion, without specific requirements as to the number, location, activity, and ownership of such labs. While some expansion may be justified to address deficiencies in lab capacity for the development of medical countermeasures, unwarranted expansion without adequate oversight is proliferation, not expansion. Since the full extent of the expansion is not known, it is unclear how the federal government can ensure that sufficient but not superfluous capacity—that brings with it additional, unnecessary risk—is being created.

The limited federal oversight that does exist for high-containment labs is fragmented among different federal agencies, and for the most part relies on self-policing. The inherent weaknesses of an oversight system based on self-policing are highlighted by the Texas A&M University case. While CDC inspected the labs at Texas A&M in April 2006, as part of its routine inspection, its inspectors failed to identify that (1) a worker became

exposed and ill; (2) unauthorized experiments were being conducted and unauthorized individuals were entering the labs; and (3) agents and infected animals were missing. It was not until a public advocacy group found out about the *Brucella* incident and, according to this group, applied pressure—by demanding records about the incident—that TAMU reported this incident to the CDC. This report prompted the subsequent in-depth investigations by the CDC.

However, this incident raises serious concerns about (1) how well the CDC polices select agent research being conducted in over 400 high-containment labs at various universities around the country, which are registered under the Select Agent Program, and (2) whether the safety of the public is compromised. Moreover, if similar safety breaches are occurring at other labs, they are not being reported. And the CDC is not finding them either. According to the experts, no one knows whether the Texas A&M incidents are the tip of the Iceberg or the iceberg.

Mr. Chairman, this concludes my prepared remarks. I would be happy to respond to any questions that you or other members of the subcommittee may have at this time.

Contacts and Acknowledgments

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Appendix I: Scope and Methodology

To determine the extent of expansion in the number of high-containment facilities and the areas experiencing the growth, we interviewed agency officials and experts, as well as reviewed documents provided by agencies and the literature.

To determine which federal agency has the mission to track and determine the aggregate risks associated with the proliferation of BSL-3 and BSL-4 labs in the United States, we surveyed 12 federal agencies that are involved with BSL-3 or BSL-4 labs in some capacity—for example, research, oversight, or monitoring. The survey requested information on the agency's involvement with high-containment labs—specifically, whether the agency has a mission to track the number of high-containment labs, whether it has a need to know, and whether it knows the number of operating BSL-3 and BSL-4 labs. The agencies that received our survey include the U.S. Department of Agriculture (USDA); the Department of Commerce; the Department of Defense; the Department of Energy; the Environmental Protection Agency; the Department of Health and Human Services (HHS), including the Centers for Disease Control and Prevention (CDC); the Department of Homeland Security; the Department of Interior; the Department of Justice, including the Federal Bureau of Investigation (FBI); the Department of Labor, including Occupational Safety and Health Administration (OSHA); and the Department of States. In addition, we sent our survey to intelligence agencies, including the Central Intelligence Agency (CIA), the National Counter-Terrorism Center (NCTC); the Defense Intelligence Agency (DIA); and the Office of Intelligence Analysis within DHS. We also met with officials of the Select Agent Program at both the CDC and the USDA to gain additional information about the expansion of high-containment labs. Finally, we reviewed documents these agencies provided, including pertinent legislation, regulation, and guidance, and reviewed scientific literature on risks associated with high-containment labs.

To develop lessons learned from recent incidents at three high-containment labs, we interviewed academic experts in microbiological research involving human, animal, and plant pathogens, and conducted site visits at selected federal, civilian, military, academic, and commercial BSL-3 and BSL-4 labs, including the sites involved in the recent incidents. Specifically, we conducted site visits to the CDC and Texas A&M University (TAMU); talked to the U.K. officials at Health Safety Executive and the Department for Environment, Food, and Rural Affairs; and reviewed documents and inspection reports.

To discuss the incidents at TAMU and the CDC, we conducted site visits and interviewed the relevant officials. We also conducted a site visit to the CDC and interviewed relevant officials, including the officials of CUH2A, Inc.—the contractor who designed the backup power system for the new BSL-4 lab in Atlanta—as well as the expert hired by this firm to conduct the reliability study for the backup power system.

We conducted our work from August 2006 through September 2007 in accordance with generally accepted government auditing standards

Appendix II: Pertinent Regulations

The regulations governing the Select Agent Program became effective on April 15, 1997, and were revised in March 2005. The regulations include six primary components: (1) a list of select agents that have the potential to pose a severe threat to public health and safety; (2) registration of facilities before the domestic transfer of select agents; (3) a process to document successful transfer of agents; (4) audit, quality control, and accountability mechanisms; (5) agent disposal requirements; and (6) research and clinical exemptions.

For facilities registered with the CDC and the USDA that possess, use, or transfer select agents, the select agent regulations require (1) an FBI security risk assessment for a number of individuals, including each person who is authorized to have access to select agents and toxins; (2) written biosafety and incident response plans; (3) training of individuals with access to select agents and of individuals who will work in or visit areas where select agents or toxins are handled and stored; (4) a security plan sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release, and designed according to a site-specific risk assessment that provides protection in accordance with the risk of the agent or toxin; (5) possible inspection by the CDC or USDA of the facility and its records before issuance of the certificate of registration; (6) maintenance of records relating to the activities covered by the select agent regulations; and (7) facility registration with the CDC or the USDA that indicates (a) each select agent that the entity intends to possess, use, or transfer; (b) the building where the agent will be used and stored; (c) the laboratory safety level; (d) a list of people authorized to have access to each select agent; (e) the objectives of the work for each select agent, including a description of the methodologies or laboratory procedures to be used; (f) a description of the physical security and biosafety plans; and (g) assurance of security and biosafety training for individuals who have access to areas where select agents are handled and stored.

Appendix III: The Select Agents and Toxins List

HHS Select Agents and Toxins

Abrin
Cercopithecine herpesvirus 1 (Herpes B virus)
Coccidioides posadasii
Conotoxins
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Ebola virus
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed 1918 influenza virus[1]
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
South American Haemorrhagic Fever viruses
- Flexal
- Guanarito
- Junin
- Machupo
- Sabia

Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses
- Central European Tick-borne encephalitis
- Far Eastern Tick-borne encephalitis
- Kyasanur Forest disease
- Omsk Hemorrhagic Fever
- Russian Spring and Summer encephalitis

Variola major virus (Smallpox virus) and
Variola minor virus (Alastrim)
Yersinia pestis

USDA Select Agents and Toxins
African horse sickness virus
African swine fever virus

[1]Reconstructed replication-competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments.

Akabane virus
Avian influenza virus (highly pathogenic)
Bluetongue virus (Exotic)
Bovine spongiform encephalopathy agent
Camel pox virus
Classical swine fever virus
Cowdria ruminantium (Heartwater)
Foot-and-mouth disease virus
Goat pox virus
Japanese encephalitis virus
Lumpy skin disease virus
Malignant catarrhal fever virus
(Alcelaphine herpesvirus type 1)
Menangle virus
Mycoplasma capricolum/ M.F38/M. mycoides Capri
(contagious caprine pleuropneumonia)
Mycoplasma mycoides mycoides
(contagious bovine pleuropneumonia)
Newcastle disease virus (velogenic)
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Vesicular stomatitis virus (exotic)

Overlap Select Agents and Toxins
Bacillus anthracis
Botulinum neurotoxins
Botulinum neurotoxin producing species of Clostridium
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei)*
Burkholderia pseudomallei (formerly *Pseudomonas pseudomallei)*
Clostridium perfringens epsilon toxin
Coccidioides immitis
Coxiella burnetii
Eastern Equine Encephalitis virus
Francisella tularensis
Hendra virus
Nipah virus
Rift Valley fever virus
Shigatoxin
Staphylococcal enterotoxins

T-2 toxin
Venezuelan Equine Encephalitis virus

USDA Plant Protection and Quarantine (PPQ) Select Agents and Toxins
Candidatus Liberobacter africanus
Candidatus Liberobacter asiaticus
Peronosclerospora philippinensis
Ralstonia solanacearum race 3, biovar 2
Schlerophthora rayssiae var zeae
Synchytrium endobioticum
Xanthomonas oryzae pv. Oryzicola
Xylella fastidiosa (citrus variegated chlorosis strain)

Appendix IV: Biological Agents Recommended for BSL-3 or BSL-4 Containment that Are Not Select Agents

There are a number of biological agents causing severe illness or death that are not select agents. For example, there are five agents that are recommended for containment at BSL-4 because of (1) their close antigenic relationship with a known BSL-4 agent and (2) the fact that there is insufficient experience working with them (see table 5).

Table 5: Nonselect Agents Recommended for BSL-4 Containment

Agent	Family
Absettarov	Flavivirus
Alkhumre	Flavivirus
Hanzalova	Flavivirus
Hypr	Flavivirus
Kumlinge	Flavivirus

Source: GAO analysis of BMBL data, 5th Edition

BMBL containment and safety recommendations for *B. anthracis*, the causative agent for anthrax and a select agent, are to include the use of BSL-2 practices, containment equipment, and facilities for clinical and diagnostic quantities of infectious cultures. However, BSL-3 practices, containment equipment, and facilities are recommended for (1) work involving production quantities or high concentrations of cultures, screening environmental samples especially with powders, and (2) for activities with a high potential for aerosol production. Safety and containment recommendations for some agents, which are not regulated under the Select Agent Program, are as strict or stricter than the recommendations for *B. anthracis*. Some nonselect agents, to which containment recommendations at BSL-3 under certain conditions apply, are listed in table 6.

Table 6: Some Nonselect Agents Requiring BSL-3 Containment under Certain Conditions

Agent	Disease
Bordetella pertussis	pertussis (whooping cough)
Chlamydia psittaci	psittacosis
Mycobacterium tuberculosis complex	tuberculosis
Neisseria gonorrhoeae	gonorrhea
Neisseria meningitidis	meningitis, septicemia
Salmonella typhi	typhoid fever
Hepetitis B, C, and D viruses	hepatitis B, hepatitis C
Human herpes virus	herpes simplex et al.
Noncontemporary human influenza strains (H2N2)	influenza
Lymphocytic choriomeningitis virus	aseptic meningitis, encephalitis
Lyssaviruses	rabies
Retroviruses	HIV
SARS coronavirus	SARS

Source: GAO analysis of BMBL data, 5th Edition

Appendix V: Description of Incidents at Texas A&M University

TAMU is registered with CDC's Select Agent Program and approved for work on several select agents. TAMU has several BSL-3 laboratories and works extensively on animal diseases, including those caused by the select agents *Brucella melitensis*, *Brucella abortus*, and *Brucella suis*. *Brucella melitensis* can cause brucellosis in humans, a disease causing flu-like symptoms such as fever and fatigue. But in severe cases, it can cause infections of the central nervous system. TAMU is also registered for use of *Coxiella burnetii*, an animal agent that can cause Q fever in humans.

According to the CDC, in February 2006, a lab worker was helping out with an experiment to aerosolize *Brucella* as a challenge for mice. The lab worker had no familiarity with the specifics of working with *Brucella*, but did have experience working with the aerosol chamber. It was determined that the lab worker got exposed to the agent during cleaning of the chamber after the experiment was run.

At the time of the exposure, neither the exposed worker nor anyone else had any indication that an exposure had taken place. In fact, CDC inspectors were on campus days after the *Brucella* exposure for a routine inspection but uncovered nothing that alerted them to the fact that an incident had taken place.[1] Symptoms did not start to appear in the exposed worker until more than a month after the exposure, and then the symptoms were flu-like. Confirmation of brucellosis was not made until another month had passed and symptoms had worsened. However, once the brucellosis determination had been made, the worker notified appropriate authorities at TAMU. But no report was subsequently made to the CDC as required by federal regulation and a year passed before—by chance—an independent watchdog group reviewing unrelated documentation,[2] acquired through the Freedom of Information Act (FOIA),[3] uncovered the lapse in reporting and forced TAMU to notify the CDC.

The subsequent investigation by the CDC revealed a number of other violations of the select agent regulations including (1) TAMU was not authorized to aerosolize *Brucella* in the first place; (2) a number of lab

[1]The CDC inspected labs at TAMU on February 22, 2006, and documented 47 facility "departures," but did not note any of the violations later uncovered.

[2]The Sunshine Project, *Mandate for Failure, The State of Institutional Biosafety Committees in an Age of Biological Weapons Research* (Austin, Texas, Oct. 4, 2004).

[3]5 U.S.C. § 552.

workers from another BSL-3 lab had tested positive for *Coxiella* antigens in their blood serum, suggesting potential exposures had taken place for that agent as well, but without reports going to CDC; (3) unauthorized access to select agents and toxins; (4) missing vials and animals; (5) and multiple protocol and procedural deficiencies across TAMU's BSL-3 labs in general.

On April 20, 2007, the CDC issued a cease-and-desist order for all work on select agents and toxins within the affected high-containment lab, as well as all aerosolization work at TAMU involving select agent and toxins. That order was subsequently expanded to include all work with select agents and toxins at TAMU—the first time the CDC has ever issued such an order entitywide under the select agent regulations. That order remains in effect as of the date of this testimony.

Related GAO Products

Export Controls: Vulnerabilities and Inefficiencies Undermine System's Ability to Protect U.S. Interests. GAO-07-1135T. Washington, D.C.: July 26, 2007.

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Plum Island Animal Disease Center: DHS and USDA Are Successfully Coordinating Current Work, but Long-Term Plans Are Being Assessed. GAO-06-132. Washington, D.C.: December 19, 2005.

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Homeland Security: CDC's Oversight of the Select Agent Program. GAO-03-315R. Washington, D.C.: November 22, 2002.

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Gage, Bill (EEA)

From: Mina Makarious [mmakarious@AndersonKreiger.com]
Sent: Friday, February 22, 2013 4:39 PM
To: Sullivan, Rick (EEA); Gage, Bill (EEA)
Cc: Valley Bartlett, Maeve (EEA); Davis, Gary (ENV); 'sjaffe@foleyhoag.com'; Laura Maslow-Armand (laurama@lawyerscom.org); 'Jennifer Rushlow'; Peter Shelley; Arthur Kreiger; Christine M. Griffin
Subject: Public Comments re BioSquare Phase II, EEA No. 12021
Attachments: Comments letter w-exhibits (A0180153).pdf; Klotz Jan 2013 full resume.pdf

Dear Secretary Sullivan:

Attached please find our comments regarding the SFEIR for BioSquare Phase II. In addition, please find a more up to date version of the resume for Dr. Lynn Klotz than the one enclosed with the paper copy of the comments submitted to your office by hand today.

Thank you.

Mina Makarious

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